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A Modern Pathological and
Therapeutical Study of

RHEUMATISM, GOUT,
RHEUMATOID ARTHRITIS
AND
ALLIED AFFECTIONS.

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EDMUND L. GROS, M. D.,

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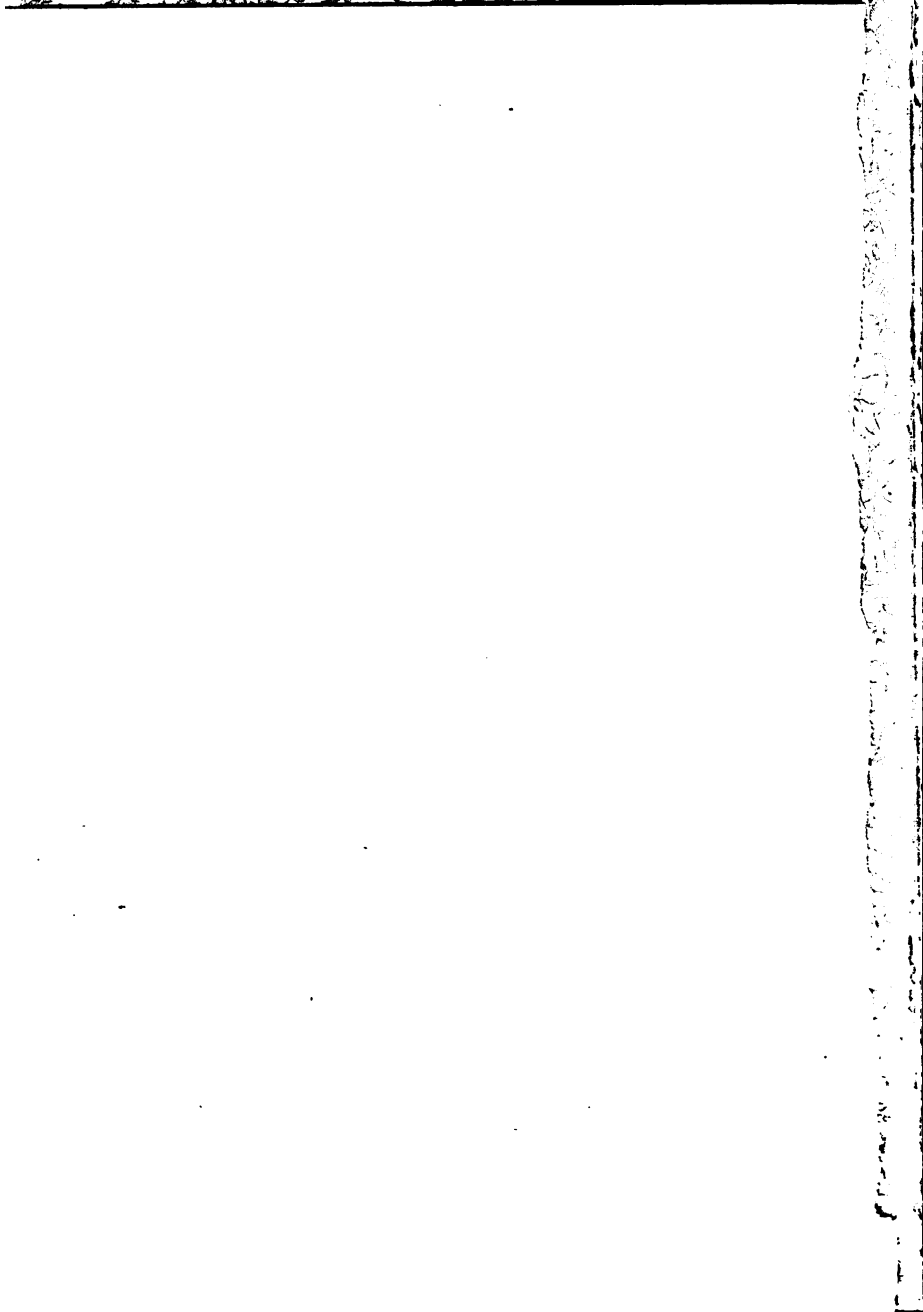
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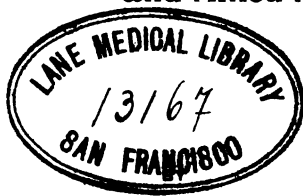
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and Allied Affections.



EDMUND L. GROS, M. D.,
OF THE FACULTY OF PARIS.
(Translated from the French.)

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GOUT, RHEUMATISM, AND ALLIED AFFECTIONS.



Are acute articular rheumatism, the various chronic rheumatisms (including rheumatoid arthritis), and gout, allied affections originating in a same morbid cause, differing only in their external manifestations and aspects, or are they widely different diseases possessing but an apparent consanguinity and a misleading clinical similitude?

In truth we experience as much difficulty in answering this question to-day as would our forefathers years ago, and strange as it may seem, in this era of marvellous discoveries and undreamed-of wealth of knowledge, this very subject is not much more advanced than in the days of Hippocrates.

The very obscurity which environs this chapter becomes an excuse for the study we propose to make. We shall draw a short historical sketch of the evolution of ideas and theories in connection with these affections, dwelling more fully on the modern appreciation of the subject, the results of recent researches and investigations and the conclusions to be drawn therefrom.

History of Rheumatism and Gout

When we study the ancient authors, we find that the word rheumatism is a very old one indeed, and that in remote times it had even a wider application than it has to-day (which is saying a great deal). It was used in connection with all pains: articular, muscular, nervous, as well as various congestions, diarrhoeas, colics etc.

All these morbid conditions were classified under the general head of *arthritism*, which really does not differ much from our modern conception of that term.

As to the distinction between gout and rheumatism, it is very probable that Hippocrates, Galien, and Paul of Aegina had not learned to differentiate these two affections, we may even doubt if the author of the term *podagra*, supposed to be Capadocia (138?), had really a distinct idea of the existence of gout, or only applied this term in connection with all articular affections of the foot.

The first precise description of gout is attributed to Coelus Aurelianus (who lived, according to the German historian, Vossius, in the second century).

The word gout (from *gutta*, a drop), comes from Radulfe (13th century), and the pathogenesis implied in that expression, a morbid matter oozing out drop by drop from the blood and clogging up the articulations, singularly approaches to the modern theories, which look for

the cause of gout in the precipitation of urates in the joints. We shall see further on, that this explanation, simple as it seems and widely accepted as it is, constitutes perhaps, a myopic view of the subject, which by no means satisfactorily explains all the phenomena attending gouty manifestations.

Separation of Gout from Acute Articular Rheumatism. To Baillou (1560) reverts the honour of having clearly separated gout from acute articular rheumatism, and, something over a century after, the famous

Sydenham wrote his memorable work, which has since remained classical, but which cost him the severest attack of the disease. In fact, the English Hippocrates, studied the disease so carefully upon himself, that very little has been left to his successors, as far as the description of the regular normal gout is concerned. He touched but lightly on acute articular rheumatism and lumbago.

Since the time of Baillou then, and especially under the genius of Sydenham, gout became a clearly defined disease, possessing a distinct clinical autonomy. Not so with rheumatic fever, however; the authors of the 18th century indulge in the strangest flights of classification. For instance, Musgrave, in 1702, speaks of rheumatism as being consecutive to chlorosis, dropsy, melancholia, asthma, fevers, colic, skin diseases. etc.

During all the 18th century the subject becomes more and more complicated. Stoll, in 1780, divides all inflammations into *rheumatic*, *bilious* and *septic*.

The question was badly muddled at the beginning of the present century, and it was not until 1840-1848 that Bouillaud in France, and Garrod in England, both possessed of wonderful clinical perspicuity, to some extent dispelled the ever thickening darkness which enveloped the subject.

Tennant and Pearson had already, in 1795, found that the gouty concretions were formed of urates, but Garrod was the first to call attention to the fact that the blood of gouty patients contains an excess of uric acid. His method of determination with the thread still renders signal services.

This uricaemia, then, according to him, is the cause of all gouty manifestations.

The pathogenesis of gout, we see, becomes clearer as we progress, but rheumatism is far from enjoying the same good fortune.

**Opinion of
older authors
on Rheuma-
toid Arthritis.**

In 1853, Charcot wrote an inaugural thesis, entitled "*Chronic progressive articular rheumatism*." (our rheumatoid arthritis), and we can ask for no better criterion concerning the state of knowledge at that time than the fact that Charcot himself proclaimed the absolute identity of acute, sub-acute and chronic rheumatism.

To explain the articular deformities in rheumatoid arthritis, *rhumatisme noueux* "knotted rheumatism," as the French call it, Charcot advanced the hypothesis of a reflex action, but he considered that the origin of the nervous irritation resided in the diseased joint.

Even at the time of the great Trousseau, this confusion still persisted, and he confesses to his pupils, at the Hotel Dieu, that his opinions are possessed of no little instability. For instance, he insists at one time on the absolute autonomy of "knotted rheumatism," or rheumatoid arthritis, and in his more recent teachings he completely modifies his first opinion and admits that this affection is also of a rheumatic nature.

We can all appreciate his embarrassment, for even to-day the relationship of rheumatoid arthritis with gout and rheumatism cannot be satisfactorily explained. In fact, the following words might have been spoken yesterday instead of thirty years ago:—

"I do not think," says the illustrious Trousseau, "that we can feel ourselves justified to-day in emitting precise and exact conclusions."

In 1875, Senator divides this subject in two chapters; in one he places acute and chronic articular rheumatism, and in the other arthritis deformans or rheumatoid arthritis and gout.

Such was the state of our knowledge a few years ago, and this rapid historical *exposé* has

served to show how far we were from that precision which assures in a subject, a clear comprehension. I fancy I hear the question: "Are we any nearer to that precision and clear comprehension to-day than were our predecessors?" The question, I think, can be decidedly answered in the affirmative. It would indeed be unfortunate if, with our modern growth of bacteriological research, nothing had been accomplished! This would almost justify the unfortunate expression of a certain French minister, who asserted that "science was bankrupt." True, the specific germ which causes acute articular rheumatism has not yet been found, but even if it should escape all our researches, we can legitimately consider that it does exist, for all our clinical testimony points to the fact that acute rheumatism is an infectious disease due to a special micro-organism.

Neither is the microbe of measles, nor scarlatina, nor syphilis known, and yet we none of us doubt their existence.

**More recent
Discoveries.**

A deeper bacteriological study of the various articular affections has led to the discovery that under certain morbid conditions, numerous microbes find in the synovial membranes of joints a favourable medium for reproduction, and it has been found that besides the normal acute articular

rheumatism there exists hybrid forms, due to various germs such as gonococcus of Neisser, streptococcus pyogenes, staphylococcus aureus, pneumococcus, etc. This has led to the forming of a side division of secondary or pseudo-rheumatisms, which have very little in common with the acute polyarthritis.

The following classification demonstrates the exact state of our knowledge to-day, and reflects more especially the opinions of the French authors:

I.—GOUT.

1. Acute articular gout.
2. Chronic gout.
3. Abarticular or visceral gout.

II.—RHEUMATISMS.

- | | | |
|-----------------------------------|---|---|
| 1. Acute forms. | { | (a). Acute febrile polyarthritis.
(b). Secondary or pseudo-rheumatism. |
| 2. Chronic forms.* | { | (a). Simple chronic rheumatism.
(b). Progressive chronic rheumatism or arthritis deformans.
(c). Partial chronic rheumatism.
(d). Fibrous rheumatism. |
| 3. Visceral or Abarticular forms. | { | This division comprises all muscular rheumatisms; neuralgia, sciatica, iritis, pharyngitis, dermatitis, pericarditis, etc.
Friedlander further classes under this head anterio-polyomyelitis, acute bulbar paralysis, Basedow's disease, diabetes, Landry's paralysis, chorea. |

It is here that we may again place the question

* We may here say that much controversy exists as to the clinical divisions of the chronic rheumatisms. Teissier

with which we prefaced this study: are these various morbid states closely connected with each other, or are they essentially and fundamentally different ?

Let us here pay *en passant* a just tribute to Bouchard, who, in his study upon the "*Maladies par ralentissement de la nutrition*," has done so much to dispel the confusion heretofore so prevalent in this very interesting question, he created the chapter of diseases resulting from retarded organic oxidations, and in it he placed gout, rheumatism, lithiasis and gravel, lithaemia, as well as diabetes, obesity, certain forms of asthma, etc.

The diathesis which Bouchard describes is identical to the *arthritis* of other authors.

Here the question naturally presents itself; what is arthritis? This is a vague term and yet it has in every clinician's mind a definite meaning; *we need vague terms to express vague morbid states!*

As we have seen, Bouchard thinks that it is a diathesis of slow combustions, Landouzy agrees with him since he calls it a *bradytrophic* diathesis. of Lyons in a recent congress (Saint Etienne, August 1897), divides the chronic rheumatisms into three groups:

1. Arthritis deformans.
2. Chronic rheumatism resulting from acute attacks.
3. Gouty rheumatism, partaking of the character of both these maladies.

Landouzy applies to it the still vague term of vaso-trophic neurosis. Hanot has attempted to give this diathesis a more comprehensive definition, and he calls it "a peculiar constitutional state characterized amongst other constituents, by a viciation, which is ordinarily congenital and hereditary, of the *connective tissue and its derivatives* which places them in a condition of least resistance."

I think it is Vidal who says that arthritism is to rheumatism what scrofula is to tuberculosis. This is perhaps a clever comparison, but it throws absolutely no light on the real *nature* of the diathesis—In scrofula there exists a special vulnerability of the *lymphatic* and *glandular* systems; in arthritis the *connective* tissue is at fault. Tubercular patients often bring into the world scrofulous children; rheumatic and gouty individuals transmit to their progeniture, arthritic diathesis.

Arthritism then may be represented by the trunk of a great tree from which spring numerous branches; each branch represents a separate disease which owes its individuality to its peculiar environment, to the idiosyncrasies of the patient, and sometimes to the presence of a special micro-organism.

If we follow up this reasoning, we can understand how a rich arthritic may become gouty, obese, diabetic; whilst the poor man, who

possesses this hereditary taint, is liable to become the victim of rheumatoid arthritis, also named, *la goutte du pauvre*. If either of these becomes exposed to sudden changes of temperature, he may become afflicted with acute articular rheumatism, or simple chronic rheumatism, for the germs have here found a favorable soil in which to develop.

**Clinical signs
of Arthritism.**

What will justify our saying that a patient is the possessor of that peculiar diathesis called *arthritism*? We can do no better than reproduce the following concise enumeration of the clinical signs accompanying this morbid condition, due to Grasset ("Consultations Médicales," 1896).

"History of past attacks of acute articular rheumatism, or acute gout : erratic pains muscular or neuralgic ; meteorological impressionability ; migrains, early baldness, eczemas and dermatoses, congestions, hemorrhages (epistaxis, hemorrhoids), sweating, impressionability of the mucous membranes, urine heavily charged with urates, urinary lithiasis, biliary lithiasis ; obesity, glycosuria, dyspepsia, chronic rheumatism, cirrhosis (various angiotic and visceral sclerotic changes), divers neurosis."

We have no intention of studying in detail all the products of the arthritic diathesis, the exigency of space forbids it, but the nature of gout

and rheumatism having led to widely different interpretations, we think a short study of the latter may prove interesting in this connection.

**What is the
nature of
Gout ?**

Garrod's discovery of an excess of uric acid in the blood has led to the widespread, generally accepted idea that in *uricæmia* or *lithæmia* resides the great active factor in all gouty manifestations. Most physicians accept that as an acquired fact to-day. In reality the problem is much more complex, and such a view is certainly open to contestation.

If an excess of uric acid is the cause of gout, how is it that in leucocythaemia and Bright's disease, notwithstanding the saturation of the blood with uric acid, these conditions are unattended with a deposit of urates in the joints, nor are they accompanied by any of the symptoms generally called gouty ?

This fact has led certain *savants* to believe that the uric acid of gouty patients possesses a peculiar instability in its chemical combinations. The experiments of Pfeiffer are interesting ; in filtering urine over uric acid crystals, he found that whilst normal urine absorbed a certain quantity of the salt, the urine of a gouty individual on the contrary deposited the greater part of the uric

acid which it contained. Could it not be, then, that the morbid complexus of symptoms instead of depending upon the *quantity* of uric acid, is rather dependent upon its *quality*? The secretions and blood would simply contain a modified uric acid, easily precipitated. This hypothesis opens a new field for study.

Bouchard energetically protests against the too general acceptance of uricaemia as the cause of all gouty manifestations ; "to ascribe to the accumulation of uric acid," says he, "not only the attack of gout, but all the morbid, varied troubles of the intermediate period, the divers congestive movements which precede, accompany or replace an attack, this, I say, is a pathological temerity."

And it seems true, the presence of uric acid is but a visible result of some deeper morbid change which the organism undergoes; it may in itself produce *certain* symptoms, but it cannot give rise to *all*. How common are the lesions of internal organs in chronic gout, and how rare is it to find deposits of urates in these organs! The source of the morbid element seems to be of a deeper and more subtle nature, and should be looked for in these minute cellular changes which constitute assimilation and dis-assimilation, in a word nutrition or metabolism.

As we yet ignore the role which the nervous system plays in the genesis of these acts, the origin of uric acid itself is shrouded in mystery.

**Uric Acid :
what is its
source ?**

During an acute attack of gout there is one point upon which all observers agree: the blood contains an excess of uric acid, and the urine a very small amount.*

We know that uric acid is the product of the incomplete combustion of the nitrogenous proteid principles, a more advanced stage of oxidation yielding urea. Concerning the real source of uric acid and urea much controversion exists ; some claim that the liver plays the active urea-producing role (Brouardel, Minkowski), others sustain that uric acid is formed in the cellular recesses of the tissues, and Kolisch thinks it results from an excessive destruction of nucleine.

Whatever the source of uric acid we must admit that its abnormal accumulation in the organism must forcibly be due to one or both of the following causes :

1. Diminished elimination.
2. Increased production. {
 - (a) By diminished oxidation (Bouchard, Berecke.)
 - (b) By increased cellular activity.

* This is not the only element in which the urine is deficient. All the toxins eliminated from the body are found in a less proportion than normally. From experiments on rabbits it has been found that it takes a much larger quantity of such a urine to kill the animal than of a normal excretion. The urine during a gouty attack is one

It appears to us that both factors must play an important role, but it seems more probable that the first scene in the series of morbid acts, is constituted by an increased production of uric acid, and that secondarily, the glomeruli of the kidneys becoming irritated by this abnormal product, lose much of their permeability. Thus a vicious circle is formed : over-production results in diminished excretion, and the acute attack of gout acts as a sort of emunctory which relieves the kidney of its excessive work. The truth of this reasoning seems to be verified by the fact that before an attack of gout the urine contains an excess of uric acid, whilst during an attack the quantity of urates is considerably diminished.

This discussion is far from being futile, for it will, in a measure, explain the action of those remarkable drugs, *colchicum* and the *salicylates*. It also teaches us that dietetic measures, in the treatment and prevention of gout, are of the utmost importance.

In the next chapter we shall consider the *treatment* of these affections.

To continue our method of study, we shall first give a rapid historical sketch of the different remedies used at various times and end with a

of *diminished toxicity*. It is probable that many of the symptoms of gout depend on the accumulation of other toxic waste-products retained in the body.

short description of the more modern therapeutic measures employed.

We borrow many of the historical details which follow, from the remarkable work of Dujardin-Beaumetz (*Leçons de Clinique Thérapeutique*, 1891). As may be expected ; diseases which have given rise to such various contending theories, possess no little heterogeneity in the methods of treatment, to which they have been subjected at different times.



Treatment.

Acute Articular Rheumatism.

Historical Sketch.

This affection, being often a self-limited disease, varying greatly in its duration with different individuals and offering no signs by which a long or short attack can be predicted, has been exposed to many different treatments, each one in turn being considered by its author, the best.

Bleeding was in vogue during a considerable time. Sydenham favoured it, and even at a much more recent date (1848) Bouillaud enforced this treatment in all its rigor. Rheumatism being in itself an anaemia-producing disease, this method was a serious error on the part of the older clinicians ; it has since been completely abandoned.

Tartar Emetic proposed by Bayle enjoyed but a short-lived favour.

It suffices to mention the treatment so much lauded by Briquet and Monneret which consisted in the administration of large doses of *sulphate of quinine*. It was not an inefficacious one, but it has been entirely dethroned by new methods.

If these internal remedies are relatively few, it is not so with those intended for external applications, and in reviewing them one wonders at the marvellous ingenuity displayed in the concoction of the various liniments, balsams, salves, etc. We cannot begin to enumerate them, yet it is perhaps interesting to note that the Fioraventi balsam (still much in vogue in France), contains not less than sixteen herbs and resins.

We cannot refrain from reproducing one formula which lacks nothing in originality :

Steel needles, 15 parts ; nitric acid, 45 parts ; dissolve and add: olive oil, 75 parts; alcohol, 60 parts.

These are antiquated and forgotten remedies, though in all probability many did possess anti-rheumatic properties. The liniments and balsams no doubt borrowed their efficacy from the friction employed in applying them; indeed we may safely say that the above formula for steel-needle oil, would become quite complete after the addition of a "*quantum sufficiat*" of what is vulgarly called "elbow-grease."

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an action in rheumatism as mercury has in syphilis and quinine in intermittent fever?

Many physicians would not hesitate to answer in the affirmative.

Oettinger ("Thérapeutique du Rhumatisme et de la Goutte," 1896) says:

"The therapeutic action of the salicylates manifests itself very rapidly in acute articular rheumatism; in a few hours the pains are amended, followed by the disappearance of the articular congestion and in a space of time which varies from one to three days, the temperature falls progressively, the movements become free and easy.

"That which proves the marvelous action of this remedy is the fact that when its administration is stopped prematurely, the painful phenomena reappear, the temperature again rises; in a word, a veritable relapse occurs. If we remember the state in which rheumatics found themselves before the use of the salicylates, the cries of pain to which they gave vent on the slightest movement of the bed, if we compare that picture with the one offered by our modern patients, so rapidly ameliorated, it is hard not to believe that a veritable specific has been found."

Bristow, Maclagen, Senator are, in fact, so persuaded of a specific action that they consider that the salicylates may be used as a means of diagnosis to distinguish the real form from the pseu-

do-rheumatisms, just as mercury and the iodides are in syphilis.

Origin of this medication, From time immemorial, plants containing salicylic acid or its derivatives, such as the bark of the *salix alba* or willow, have been used in the treatment of intermittent fever, and an infusion of a species of willow seems to have been long extensively employed in Southern Africa by the Hottentots, in the treatment of rheumatism.

How do the Salicylates act? We have no intention of entering deeply into the physiological action of the salicylates. Extensive experimentation has been made to discover their exact mode of action, but notwithstanding these researches, authors are still far from agreeing on many points.

The following appears to us the most rational explanation of the action of the salicylates in rheumatism.

It is necessary to remember in this connection, that salicylic acid possesses very strong antiseptic properties, equal or even superior to carbolic acid. Salicylate of soda, on the contrary, according to Kolbe, is devoid of antiseptic power.

The knowledge of these facts is indispensable for the clear comprehension of the following theory, which we must admit, seem to explain sat-

isfactorily many of the drug's therapeutic properties (Nothnagel and Rossbach). Salicylic acid, whether administered as such or in the form of its salts, is always converted into salicylate of soda in the blood. In a normal individual there exists an insufficient quantity of carbonic acid in the blood to liberate salicylic acid from its salts, but if experimentally or pathologically there is an increase of this gas, the acid is freed from its chemical combinations and regains its free state.

Kohler has attained these conditions in the laboratory by using the blood of a suffocated animal. Now, under certain pathological conditions, the tissues themselves contain an excess of CO_2 which readily decomposes the salicylate of soda. In a violent local inflammation, then, such as is produced by an attack of acute articular rheumatism, a nascent acid is formed at the very seat of the lesion, and a powerful antiseptic action is exerted.

This would explain also the efficiency of the salicylates in other local inflammations, such as tonsillitis, iritis, urethritis, etc.

We have insisted at some length on the antiseptic properties, because these most satisfactorily explain the remarkable potency of the drug in acute rheumatism, but we cannot pass in silence its *antithermic, cholagogic and eliminatory* qualities. In febrile affections, the salicylates reduce temperature as effectively as sulphate of quinine.

It is the only drug which liquefies the bile and at the same time increases its flow.

Perhaps to its eliminatory powers is more especially due its favourable action in gout and chronic rheumatism. Its administration is not only followed by a slight diuresis, but also by a marked increase of all solid constituents of the urine, especially *urea* and *uric acid*. When we realize that salicylic acid is an *antiseptic*, an *eliminator*, a *cholagogue*, an *antithermic*, and, according to some, an *analgesic*, we no longer wonder at the efficacy of its action in rheumatism (acute and chronic), rheumatoid arthritis, muscular rheumatism, lumbago, neuralgias, sciatica, gout and even the fulgurating pains of locomotor ataxia!

To what may be attributed the occasional irregularity in their action, If the salicylates were considered a few years ago as absolute specifics by such men as Stricker, G. See, Dujardin-Beau-metz and many others of equal celebrity, how is it that modern observers are less unanimous in their praise, and how can we explain that the results obtained are frequently unsatisfactory, and sometimes absolutely harmful? We think that the answer to this question must be sought for in two factors, viz.:

1. The salicylates have been administered in pseudo-rheumatisms.

2. The artificial *synthetical* salicylates are almost exclusively used to-day, whereas, the earlier experiments were made only with salicylates obtained from wintergreen, sweet birch, willow bark, salicine and other natural sources.

We have seen that alongside

1. The Salicylates in pseudo-rheumatisms. the real acute articular rheumatism are numerous other arthritides, improperly called also rheumatisms, which are due to various morbid germs, recently isolated in the inflamed joints.

The salicylates have rarely any action in these cases. The specific germ of acute polyarthrititis is probably much more sensitive to the action of salicylic acid than are these other micro-organisms.

These facts, which serve to explain some of the failures of the salicylates, should, however, not prevent us from trying them in *every* case of acute joint disease, even though it be manifestly secondary; for, as Manquat justly remarks ("Thérapeutique," 1896, p. 292), if articular symptoms make their appearance during an infectious disease, such as scarlatina, gonorrhœa, mumps, etc., we must not immediately conclude that we have to deal with an arthritis partaking of the nature of the above diseases. *An infectious disease may awaken a dormant rheumatic tendency*, and many cases of

so-called secondary, or pseudo-rheumatism are really attacks of genuine acute articular rheumatism, susceptible of rapid amelioration under the influence of the mixed treatment (the salicylates and colchicine).

This treatment even offers a therapeutic distinction between the two forms. In *all cases* of acute joint disease, a few doses of colchi-sal or colchicine (methyl) salicylate,* would constitute an excellent means of diagnosis, and perhaps would often give unexpected successes.

II. Physiological divergencies between artificial and natural salicylate.

Kolbe, in 1874, discovered a method by which a salicylic acid could be obtained (by the action of carbonic acid on the phenylate of soda). This cheaper artificial acid, has of course rapidly replaced all the natural salicylates. In its chemical and physical reactions it is identical with the salicylic acid derived from the oil of gaultheria, betula lenta, meadowsweet and other plants, and yet it is far from possessing the same therapeutic value; in fact, *it often exerts a violent toxicity*. This, perhaps, explains why the remedy fails in just such cases as should be rapidly amended. This fact is generally ignored, and we think it worth the while to insist upon it, especially as

*A solution of crystallized colchicine, in natural methyl salicylate.

much has been discovered through recent investigations.

The superiority of the *natural* product, and more especially of the methyl salicylate over the *artificial* salicylates is admitted by most authors, but the toxic effect attending the administration of the latter is perhaps too lightly touched upon.

Lauder Brunton, in his great work on therapeutics ("Pharmacology, Therapeutics and Materia Medica, London"), says: "The salicylic acid prepared from salicin or oil of wintergreen is purer than that made artificially, and may frequently be tolerated by patients when the artificial acid disagrees."

Potter ("Handbook of Materia Medica, Pharmacy and Therapeutics," 1890, p. 349) makes practically the same statement.

Manquat (*loc. cit.*) claims that the oil of gaultheria and of betula lenta (which is a pure salicylate of methyl), is more antiseptic than salicylic acid, possesses all the anti-rheumatic properties of salicylate of soda, is at the same time much less toxic, and produces hardly any irritation.

The first precise experiments on animals we owe to Prof. Charteris, of Glasgow. The results he has obtained are of the deepest interest.

In his experiments on rabbits he found that the *artificial* salicylic acid in 10-grain doses, and sodium salicylate (from the artificial acid) in 18

grain doses, promptly killed rabbits weighing $2\frac{1}{2}$ pounds.

The best specimen of artificial acid sold as chemically pure, proved fatal in 15-grain doses to one rabbit, whilst, on the contrary, salicin in 30-grain doses, natural salicylic acid in 10-grain doses and sodium salicylate (from the natural acid) in 30-grain doses, had absolutely no deleterious effect on rabbits weighing $2\frac{1}{2}$ pounds.

The dangerous effect of the artificial product is due, according to Prof. Charteris, to the presence of cresotic acid, parahydroxybenzoic acid and hydroxyisophthalic acid (Extracted from an article by William F. Waugh, in the "Times and Register").*

We, personally, have used *natural* methyl salicylate in some cases where the commercial salicylate of soda absolutely failed, or in which its administration was attended with very disagreeable visceral symptoms, and have obtained excellent results.

Two remedies which seem to mutually aid and complete each other's action, are colchicine and methyl salicylate. We shall study the physiological action of colchi-

Association of Colchicine and the Salicylates.

* As the presence of these toxic substances can only be determined by very delicate chemical tests on large quantities of material, artificial salicylates can only be detected by their disappointing physiological results, and in the manufacture of the commercial salicylates, it is impossible to eliminate these dangerous impurities.

cum in connection with gout; we shall also see that it possesses many traits which make it useful in rheumatism as well, a fact already demonstrated by Badia, who years ago used hypodermic injections of colchicine in rheumatism, and more recently utilized by Heyfelder of St. Petersburg.

We know of no better combination than the following formula, dispensed in gelatine capsules, each containing $\frac{1}{4}$ a milligramme (1-260 grain) of colchicine, and 20 centigrammes of the natural methyl salicylate distilled from the *betula lenta* (N. O. Amentaceæ).

It is essential, when exhibiting these remedies, to properly divide the doses, and small capsules which can be administered every hour, or every alternate hour, admirably fulfil this *desideratum*.

That this combination, whose commercial cognomen is *colchi-sal*, is more active than the salicylates alone, is proved by the fact that in *chronic rheumatism* (which is almost universally considered as not being amenable to the salicylates), remarkable results have been obtained.



Treatment of Gout and Lithemia or so-called American Gout.

Alkalies. Notwithstanding the fact that before the discovery of uric acid in the urine and blood, our predecessors must have ignored that gout is a disease of an acid diathesis, alkalies were administered empirically. The old authors prescribed a decoction of the vegetable ashes.

This is really the origin of the alkaline treatment, which still enjoys to-day a well-earned reputation. They find their special indication in the first progressive stages of gout, but are absolutely contra-indicated when the disease has attained the chronic stages, with tophi and general depression.

The alkalies can never become, even in the first stages of gout, a curative remedy, but they are valuable adjuvants in connection with other more active medicaments.

Colchicum and the Salicylates. There are two drugs which in the treatment of gout, and especially of the acute attack, possess really remarkable powers; we speak of the *salicylates* and *colchicum*.

We have already insisted upon the action of the salicylates in connection with rheumatism; we have seen that they increase the elimination of urea and uric acid, reduce pain and temperature,

increase the flow of bile, and we have no difficulty in understanding their efficiency in gout.

Perhaps no drug in the Pharmacopœia possesses as expeditious and remarkable an action as colchicum. Under its influence an acute attack of gout is dispelled as if by magic. We cannot be surprised that a drug of such powerful efficacy should have often been used injudiciously, and as a result have, at one time or another, fallen into disfavour.

Let us study more in detail the drug which was condemned by the great Sydenham, Trousseau, Cullen and Todd, and praised to the skies by Garrod, Dyce Duckworth, Lecorché, and so many others.

Is Colchicum a Specific? Garrod was not afraid of affirming that colchicum exercises as specific an action over gout, as cinchona exerts over intermittent fever. Dyce Duckworth, during fifteen years, prescribed colchicum almost exclusively to all his gouty patients, and claims never to have had cause to regret it. Lecorché, who, perhaps, of all modern scientists, has made the most complete study of gout says: "With no remedy have we obtained with our gouty patients such constant, rapid and decisive results as with colchicum, and we do not hesitate in saying that the cure, not only of articular affections, but also of any visceral manifes-

tion by the use of colchicum, is an indisputable proof of the gouty nature of that manifestation."

In face of these praises it is but justice to quote the words of Trousseau: "During the last thirty years, I have observed a considerable number of gouty patients. In the beginning of my practice, I, like many others, attempted to fight against the disease; to-day I remain with folded arms; I do nothing, absolutely nothing, to relieve an acute attack of gout."

It was retrocessive gout that Trousseau feared, and he believed in a metastasis. To-day we know that the visceral symptoms are due to uremic poisoning; we know then that the kidneys are not doing proper work, and we can shape our therapeutics accordingly. We are not justified in remaining like Trousseau, with arms folded, nor in following the precepts of Cullen, contained in those two words, *patience* and *flannel*. It is active intervention the patient cries for, and active intervention that modern research justifies our giving. All physicians now agree on this point, though there exists some controversy as to the moment at which we should administer our remedies. Bouchard waits until the articular symptoms become attenuated; on the contrary, Lecorché exhibits his colchicum immediately. We think that some discrimination should be used, and that the best criterion lies in the state of the urine. If the kidneys do their work well, the sooner the attack of gout is dissipated the better.

**Association
of Salicylates
and
Colchicine.**

Here again a combination of those two most valuable remedies, salicylates and colchicine, will be found of the greatest benefit. We speak of *colchicine* and not *colchicum*, because recent experiments have proved that this alkaloid possesses all the properties of the colchicum seed or corne, without offering any of the inconveniences of the uncertain preparations made from the plant. The physiological strength of the tincture or wine varies to a very great extent, the alkaloid alone can be mathematically dosed, and its effects accurately controlled.

It seems to us that not enough has been said of this association of drugs, the type of which exists in *colchi-sal* capsules.

It is a very remarkable fact that when salicylate of methyl is associated with colchicine, effects may be obtained that would necessitate a much larger dose of either of the drugs used isolately. We see by the following comparative tableau how admirably the action of the one drug is seconded by the other.

SALICYLATE OF METHYL.
1. Increases the elimination of urea, uric acid and other solid constituents of the urine.

COLCHICINE.
1. Diminishes the production of uric acid (Graves)
2. Promptly increases elimination of all waste pro-

- | | |
|--|--|
| <ul style="list-style-type: none"> 2. Quiets Pain. 3. Liquefies and increases flow of bile. 4. Slightly diuretic. 5. Diaphoretic. 6. Reduces fever. 7. Combats congestion and facilitates resolution of inflammation (G. See). 8. Antiseptic action in the blood. | <ul style="list-style-type: none"> ducts and promotes tissue oxidation (Bartholow). 3. Quiets pain. 4. Increases flow of bile. 5. Slightly diuretic. 6. Diaphoretic. 7. Purgative. |
|--|--|

If we take into consideration these various actions, we may safely say that the combination of these two drugs finds a very wide application. In every condition attended with, or depending on the accumulation of waste or toxic material in the organism, the above association will be found invaluable; this applies to gout, acute and chronic rheumatisms and to all affections partaking of their nature. Though the congestion and torpidity of the liver may not constitute an essential factor of these diseases, they nevertheless play a very important rôle; no more effective treatment can be found for increasing the flow of bile and unloading the portal circulation than small doses of colchi-sal, hence its indication in plethora, constipation, hepatic and cardiac dropsy. (Bartholow.)

**Dangers
attending the
administration
of Salicylate
of Soda and
Colchicum
preparations.**

We must here say a few words concerning the accidents which have sometimes followed the exhibition of salicylate of soda as well as colchicum, and which have been the cause that these drugs are looked upon with considerable suspicion, especially by the younger generation of physicians. These accidents, consisting in a violent congestion of the kidneys, various digestive troubles, tinnitus, aurem, vertigo, delirium, were erroneously thought to be a necessary accompaniment of the medication. For instance, G. Sée was not satisfied in his administration of salicylate of soda unless he obtained ringing in the ears, and believed it was only then that the drug acted efficiently. We know now that many, if not all of these disagreeable symptoms are due to toxic principles contained in the drug, and that these can be avoided by the use of the pure salicylate of methyl such as may be obtained from the *betula lenta*, and is exclusively used in the manufacture of colchi-sal.

It stands to reason that the smaller the dose used, the less danger there is of accidents, and when two drugs of a very similar therapeutic action are associated, a maximum of effect is obtained, with a minimum quantity of each drug.

Colchicum itself is violently irritating to the mucous membrane of the stomach, and also to the parenchyma of the kidneys, but its alkaloid, colchicine, in its therapeutic doses, seems to be free from the evil qualities of the plant. Potter asserts that the alkaloid is the best preparation and immensely superior to the tincture and wine. Laborde and Houdé condemn all wines of colchicum, as they are never of a uniform composition. The same is true of the tincture.

**Inocuity of
Colchicine
and pure
Methyl-
Salicylate.**

Colchicine constitutes the only scientific and exact method of administration. When we consider that $\frac{1}{4}$ of a milligramme only is exhibited at a time, we can conceive with what facility it is eliminated, and what insignificant local irritation it produces on the stomach and kidneys.

The doses contained in the colchi-sal capsules are $\frac{1}{4}$ milligramme of colchicine and 20 centigrammes of pure methyl salicylate. It is rarely necessary to administer more than ten or twelve capsules a day; this brings the daily dose to $2\frac{1}{2}$ milligrammes of colchicine, and 2 grammes of methyl salicylate, equivalent to 30 grains of salicylate of soda, and this dose, in its therapeutic efficacy is equivalent to 120 grains of ordinary salicylate of soda and 60 minims of tincture of colchicum.

It may here be mentioned that with the colchisal capsules, the best results are noted after slight catharsis has been produced.

Arthritis deformans, or rheumatoid arthritis, whatever its nature, is one of the affections*

Rheumatoid Arthritis. which is the most refractory to treatment. Most physicians, conscious of their weakness, make no attempt to arrest the progressive and invading march of lesions—lesions which soon constitute incurable infirmities and condemn the unfortunate patient to total impotence. Jaccoud in France, and Wood in America, do not take such a pessimistic view of the situation. They both claim to have obtained good results from the salicylates. It is here that *colchi-sal* really shows its superiority. It counts many successes where all other drugs have absolutely failed. Of course the deformities once constituted cannot be dissipated, but the progress of the disease may sometimes be arrested, and the pain always very rapidly relieved.

* Teissier of Lyons (Congres de St. Etienne, 1897), calls it an infectious tropho-neurosis. He thinks that the mould of damp habitations should be incriminated. Autopsies have revealed a meningo-myelitis, perhaps due to some cryptogamic parasite, which is probably the cause of the various deformities, so well described by Charcot.



**A FEW
PRACTICAL PRESCRIPTIONS
FOR THE
Treatment of Gouty and Rheumatic
Affections.**

Rheumatism.

I.—*Acute Articular Rheumatism.*

a.—Absolute rest in bed.

b.—Exclusive milk diet, a cup every two hours. At least three quarts a day.

To each cupful add one of the following powders :

℞ Sodii Bicarb. 3 iij

Div. in pulv. No. xx.

c.—Every other hour take one of the following capsules :

℞ Caps. Colchi-Sal No. 50

Sig. Ten or twelve a day.

d.—In the intervals, to appease the thirst, drink freely of the following infusion:

℞ Tritici Repens 3 vi
 Aquæ ℥ij
 To which has been added
 Potass. Nitrat. 3 ss.

e.—As a local treatment, wrap the affected joints in flannel, after having annointed them with

℞ Betul-ol * 3 vi

f.—If there exists persistent hyperpyrexia or marked cerebral symptoms, immediate resort to cold sponging, cold pack or cold baths.

II.—*Sub-Acute Articular Rheumatism and Simple Chronic Rheumatism.*

a.—Mixed *régime*, meat and vegetables, with a marked predominance of the latter. Avoid fats, high game, cabbage, tomatoes, sorrel. Drink milk or lemonade during meals.

b.—Until the pains have disappeared, take three capsules three times a day of

℞ Caps. Colchi-Sal, No. 50.

Then substitute to this treatment the following:

℞ Potas. Iodid. 3 iij
 Aquæ distill. ℥ ix
 Sig. A tablespoonful at each meal.

* Betul-ol (Lin. Methyl. Salicyl. Comp.) or compound liniment of methyl salicylate, which is absorbed by the skin almost immediately, and may be traced in the urine five minutes after application.

c.—During the administration of the iodide, take at the end of every week, one or two of the following pills on retiring:

℞ Pulv. Aloë Socot. gr. x
 Ext. Belladonnæ gr. ij
 Saponis q. s. ut ft. massa.
 Misce fiat in pil. no. xx. div.

d.—Every morning general friction over all the body with a stiff horsehair glove.

e.—As a local treatment, paint the affected joints with tincture of iodine, or friction them with the following liniment:

℞ Betul-ol.	} aā 3 iij
Acid. Oleici	
Olei Terebinth.	

m

III.—*Abarticular Rheumatism.*

In the following various localisations the anti-rheumatic medication is frequently very effective:

Myalgias. Lumbago, torticollis.

*Neuralgias.** Sciatica, trigeminal and occipital neuralgia, intercostal neuralgia, etc.

Phlegmasias. Pericarditis, endocarditis, endarteritis, iritis, pharyngitis, etc.

The very acute forms of muscular rheumatism

* In this group may be placed the neuralgic pains so often following grippe. They often depend on a dormant rheumatic tendency momentarily awakened by this infectious disease. Colchi-Sal and Betul-ol locally, have here a decidedly favourable action.

1. The first step in the process of the
 2. second step is the third step
 3. the fourth step is the fifth step
 4. the sixth step is the seventh step

5. The eighth step is the ninth step
 6. the tenth step is the eleventh step

7. The twelfth step is the thirteenth step
 8. the fourteenth step is the fifteenth step
 9. the sixteenth step is the seventeenth step
 10. the eighteenth step is the nineteenth step

11. The twentieth step is the twenty-first step
 12. the twenty-second step is the twenty-third step

13. The twenty-fourth step is the twenty-fifth step
 14. the twenty-sixth step is the twenty-seventh step
 15. the twenty-eighth step is the twenty-ninth step
 16. the thirtieth step is the thirty-first step

Pharmaceutical - Forms.

The first step in the process of the
 second step is the third step
 the fourth step is the fifth step
 the sixth step is the seventh step

having frequently a fatally progressive march, rarely influenced by drugs. Salicylate of soda and colchicum, as well as arsenic and iodide of potassium, are nearly always powerless to modify the evolution of the disease.

A most annoying symptom for the patient is the continual pain, which undergoes frequent exacerbations, which often render the suffering intolerable. If these pains could be controlled without the use of opiates the general condition would be much improved, and that in itself would have a tendency to retard the progress of the disease.

Colchi-sal has a very decided action on the symptom *pain*, which in many cases disappears entirely after the exhibition of a few capsules; it cannot straighten crooked joints once they are constituted, but it does certainly prevent the appearance of new deformities.

As this disease is often an accompaniment of physical decrepitude, much benefit can be obtained through the use of tonics, and especially iron, quinine and strychnine. For the already existing deformities and joint-stiffness, dry heat applied locally appears to have been followed by amelioration. Recently, in England, over-heated air, applied to the part by means of cylinders, has been attended with some remarkable results.

Gout.

I.—*Acute Articular Gout.*

a.—The first indication is rest, and it is preferable to insist upon the patient's remaining in bed.

b.—The milk diet should be exclusive, a cup every two hours, three quarts a day. To each cup add one of the following powders:

℞ Potass. Bicarb. 3 ij
Div. in pulv. No. xx.

c.—Take every hour one of the following capsules. Continue until the pain and swelling subside, or until there appear symptoms of intolerance, viz. diarrhœa and vomiting.

℞ Caps. Colchi-Sal No. 50
Sig. One every hour.

N. B. A slight laxative effect is a favourable omen and is a proof that the drug is acting properly.

d.—Envelope the joint with cotton or flannel and oiled silk after having anointed it with the following mixture (modified from the original formula proposed by Dyce Duckworth).

℞ Atropin. Sulph. gr. ij
Morph. Hydrochlor. gr. vj
Acid. oleici. ℥ js
Betul-ol ℥ ss
Misce Sig. For use as a liniment.

II.—*Chronic Gout.*

a.—If there is a general cachetic condition, no very

severe *régime* can be enforced. The first indication is to improve the general health, and to obtain this result a rather liberal diet may be permitted. If on the contrary the patient remains strong and vigorous, the meals should consist of eggs, cooked vegetables and milk; no meat.

b.—Alternate, week by week, the following treatment: During the first week take three times a day with meals, three of the following:

℞ Caps. Colchi-Sal No. 50
Sig. Eight to nine a day.

The second week replace these by the following;

℞ Lithii Benzoat 3 ij.
Extract. Gentian. q. s.
F. pil. No. 50
Sig. Two, twice a day during meal time.

The third week renew the colchi-sal, etc.

c.—A half hour before each meal take one of the following powders in some effervescent water

℞ Sodii Bicarb. 3 vij
Div. in pulv. No. xx.
Or a half glassful of Vichy water.

d.—Paint the affected joints with tincture of iodine, or rub them with the following liniment:

℞ Betul-ol. 3 vj
Alcohol. Absolut. ℥ iij
Acid. Oleici 3 iij
Misce Sig. Use as a liniment.

e.—On retiring every night, drink a glassful of hot water.

f.—Once a week take a purgative pill of aloes.

III.—*Gouty Diathesis without any actual gouty manifestations.*

Here the *régime* and diet play the all-important rôle, and as an ounce of prevention is worth a pound of cure, every individual who, through heredity or past offences against nature, is threatened with gout, should submit to the following dietetic rules and treatment.

Though no iron-bound *régime* need be instituted, the following rules must be obeyed:

a.—Never take more than three meals a day.

b.—A meal should never be copious. Habits of extreme sobriety should never be departed from.

c.—Nearly all foods may be eaten in moderation, nevertheless the following articles are prohibited:

Vinegar and all sauces, and dishes containing them. Salad should be taken without vinegar.

The following vegetables are harmful: potatoes, tomatoes, sorrel, spinage, chestnuts.

Sugar, spices, pastry should be indulged in sparingly.

d.—Drinks; in this diathesis, alcohol is man's worst enemy, for it produces the very state on which gout is supposed to be dependent viz.: *slowing of nutrition*. Water is the best of all drinks. A little light red wine may be indulged in, but strong liquors should be absolutely and totally banished.

e.—Open air life, avoid protracted intellectual efforts and *violent* bodily exercise. An intense fatigue has often precipitated a first attack of gout.

If, notwithstanding all these precautions, or on account of some neglect in diet, symptoms should

make their appearance, such as: dyspepsia, headache, articular and muscular pains indicative of gouty toxæmia, an anti-gout remedy should be taken. A combination of colchicine and the salicylates have been found very effective in warding off an attack of gout or in dissipating the pains or various derangements, due to an excessive accumulation of toxic principles in the organism.

We should, therefore, prescribe colchi-sal, six capsules to be taken daily with milk, until entire disappearance of the symptoms.

IV.—*Abarticular Gout.*

(“Goutte larvée” of French authors.)

Lecorché has shown that many headaches, neuralgias, vertigo, certain cystites, false angina pectoris, asthma, myalgias, dyspepsias, etc., when dependent on a gouty diathesis disappear rapidly under a proper anti-gout treatment.

In all the above conditions, when the gouty nature is suspected, six to eight colchi-sal capsules should be administered daily. It will constitute an excellent means of diagnosis, for in all cases due to the gouty toxæmia, the symptoms will rapidly disappear.

Prescribing Memo.

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Substitution of commercial brands of so-called "colchicine salicylate" for genuine Colchi-Sal, may be avoided, by prescribing *original bottles only* of 50 or 100 capsules.

R. Colchi-Sal : 20 centigrammes.

ft. Capsulae.

Mitte 50 (original bottle).

Sig. One capsule every hour (or as otherwise directed).

R. Betul-ol ̄ij

Sig. For external application as directed.

In the absence of distinctive chemical tests, inferior preparations and artificial salicylates can *only be detected* by their disappointing physiological results.



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